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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/729,795	WALTERS, IAN	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2007 and 05 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8,10-17,19,20 and 24-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,10-17,19,20 and 24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-5-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments to the specification and claims, filed April 12, 2007, as well as applicant's IDS filed April 5, 2007 are acknowledged.

   Claims 2, 3, 9, 18, 21 and 22 have been canceled.

   Claims 1, 4, 15-17, and 19 have been amended.

   Claims 27-30 are new.

   Claims 1, 4-8, 10-17, 19, 20 and 24-30 are pending.

   Claims 1, 4-8, 10-17, 19, 20 and 24-30 are under consideration as they read on a method for treating ulcerative colitis with anti-CD3 antibody wherein the disease activity index species is "MTWSI" and the additional agent species is "methylprednisolone".

2. This Office Action is in response to Applicant's amendment and remarks, filed April 12, 2007, as well as applicant's IDS filed April 5, 2007.

   The rejections of record can be found in the previous Office Action, mailed January 9, 2007.

   Applicant's provision of a sequence listing for SEQ ID NOs: 1-5 is acknowledged.

   The previous objections to the claims have been withdrawn in view of the amendment.

   The previous rejection under 35 U.S.C. § 112, 2nd paragraph has been withdrawn in view of applicant's amendment.

   The previous rejections under 35 U.S.C. § 112, 1st paragraph have been withdrawn in view of applicant's amendment.

   The previous rejection under 35 U.S.C. § 102(b) has been withdrawn in view of applicant's amendment.

   New Grounds of Rejection are set forth below.

3. The IDS filed April 5, 2007 has been considered.

4. The amendment filed April 12, 2007 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: a new sequence listing was submitted, however, and as stated in M.P.E.P. § 608.01(p), when applicant is inserting material previously incorporated by reference into the specification, "a statement that the material being inserted is the material previously incorporated by reference AND that the amendment CONTAINS NO NEW MATTER is also required. 37 CFR 1.57(f)."

   Applicant is required to cancel the new matter in the reply to this Office Action.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

   > The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 4, 5, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the instant claims are dependent on canceled claims.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

   > The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 15, 16, 17 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

   In particular, the claims refer to various polypeptide sequences represented by their SEQ ID NOs:, however these polypeptide sequences are considered new matter for the reasons given in Section 4 above.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

   > (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. **Claims 1, 4-8, 10-17, 19, 20 and 24-26 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Tso et al. (U.S. Patent No. 5,834,597) in view of Lobb et al. (U.S. Patent No. 5,932,214), Rutgeerts et al. (Eur J Surg. 1998 Dec;164(12):911-5), Banerjee et al. (USSN 10/622,932) Strom et al. (Therapeutic Immunology edited by Austen et al., Blackwell Science, Cambridge, MA, 1996; pages 451-456), and

further in view of Norman et al. (Transplantation. 2000 Dec 27;70(12):1707-12), Trajkovic V., (Current Opinion in Investigational Drugs 2002 3(3):411-414) and "Protein Design Labs (PDLI) Begins Phase I Clinical Trial of Nuvion in Ulcerative Colitis", (PRNewswire-FirstCall, July 9, 2002, pages 1-2, cited with applicant's IDS of August 30, 2004),

each of which (Norman, Trajkovic and PDL) ***are being cited in direct response to applicant's arguments and provision of evidence concerning unexpected results and Ulcerative Colitis clinical trials***.

This is a New Grounds of Rejection.

Applicant argues, "[t]he Tso reference mentions inflammatory bowel disease only as one of a list of many diseases, and does not specifically refer to ulcerative colitis, much less severe steroid refractory ulcerative colitis."

Applicant's argument has been considered but has not been found convincing, essentially for the reasons of record.

With respect to the teachings of Tso, as stated in the previous Office Action of January 9, 2007, Tso teaches a method of treating inflammatory bowel disease in a patient comprising administering a "therapeutically effective dose" of anti-CD3 antibody is "an amount sufficient to cure or at least partially arrest the condition and its complications," ***i.e., an amount sufficient to reduce symptom severity or cause disease remission*** (see, in particular column 12, 3rd paragraph).

The claimed invention differs from the teaching of Tso in the ***explicit recitation*** of a particular disease activity index ("MTWSI"), in the treatment of ***severe steroid-refractory ulcerative colitis***, and in the further administration of ***methylprednisolone***.

In pointing out that Tso does not teach the treatment of the treatment of ***severe steroid-refractory ulcerative colitis*** with anti-CD3 antibody applicant is merely pointing out the obvious. Applicant has not addressed why Tso, in view of the other applied references, fails to teach the claimed invention, and one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The absence of these teachings in Tso are made up by the teachings of Lobb, Rutgeerts, Banerjee and Strom. Moreover, one of ordinary skill in the art would have been motivated to combine these references, and have had a reasonable expectation of success in doing so, essentially for the reasons of record. In brief, essentially as stated in the prior Office Action of January 9, 2007, one of skill in the art would been motivated to treat severe-steroid refractory ulcerative colitis patients who are refractory to corticosteroids and would have had a reasonable expectation of success in doing so given the teaching of Tso regarding the use of anti-CD3 antibodies to treat Inflammatory Bowel Disease and further given that, as taught by Rutgeerts, the Ulcerative Colitis patient population is in great need of new treatment options, and as taught by Strom, by simultaneously combining several agents directed at different molecular targets, for example anti-CD3 in combination with a corticosteroid, one can achieve additive-synergistic effects through the application of each agent at relatively low dose, thereby limiting the toxicity of each individual agent while increasing the total immunosuppressive effect, which one of ordinary skill in the art would appreciate could in turn overcome the steroid resistance. Additionally, it would have been prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose since the idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Applicant further argues that the patient population to be treated, i.e., severe steroid-refractory Ulcerative Colitis patients, were seeking alternative forms of treatment, and "the immune system is complex and antibodies other than those listed by Rutgeerts are available to suppress many of its components and processes," and according to the NIH website of clinical trials, 72 trials employing various agents to treat ulcerative colitis are currently in progress. Moreover, applicant asserts, "clinical trials are expensive and time consuming to conduct and most do not result in an approvable product."

Based on this, applicant concludes, "...the skilled person was still left with many possible avenues that could have been explored not knowing which would be successful. Given the expense and uncertain outcome of conducting clinical trials, the difficulty of treating a condition that by definition is resistant to treatment with steroids, the skilled person would not have provided a reasonable expectation of success that the presently claimed methods would have been successful."

Applicant's arguments have been considered but have not been found convincing.

With respect to applicant's assertion that severe steroid-refractory Ulcerative Colitis patients were in need of treatment alternatives, this is indeed the case, and it is a motivating factor to combine the cited references as stated in the prior Office Action.

With respect to applicant's assertion that "the immune system is complex and antibodies other than those listed by Rutgeerts are available to suppress many of its components and processes," this is not contested, for example Tso teaches the use of anti-CD3 antibody to do so.

However, with respect to applicant's evidence for the complexity of the immune system, in particular the complexity of treating Ulcerative Colitis, i.e., the 72 currently pending clinical trials to treat ulcerative colitis according to applicant, applicant has not pointed out what, in particular, these 72 clinical trials teach with respect to state of the ulcerative colitis treatment art as of applicant's earliest claimed priority date, December 5, 2002. Indeed a random sampling of the Ulcerative Colitis clinical trials by the Examiner at the link provided by applicant indicates that many were initially posted after December 5, 2002. Moreover, it appears that applicant's argument is already outdated in that the website now lists 62 currently pending clinical trials to treat ulcerative colitis.

Furthermore, applicant asserts that in light of the fact that "clinical trials are expensive and time consuming to conduct and most do not result in an approvable product," and "the expense and uncertain outcome of conducting clinical trials and the difficulty of treating a condition that by definition is resistant to treatment with steroids," a skilled person would not have a reasonable expectation of success of practicing the claimed method as taught by Tso in view of Lobb, Rutgeerts, Banerjee and Strom.

Applicant's arguments have been considered but have not been found convincing.

In direct response to applicant's arguments and provision of evidence concerning Ulcerative Colitis clinical trials, and in direct contrast to them, the Examiner submits that at least some skilled artisans, namely Protein Design Labs, Inc., the assignee of Tso 5,834,597 according to the issued patent, did make plans to initiate a Phase I trial of anti-CD3 to treat Inflammatory Bowel Disease as of at least December 4, 2000 as taught by Trajkovic V., Current Opinion in Investigational Durgs 2002 3(3):411-414, see entire document, in particular page 411, left column, 5th paragraph. Furthermore, Protein Design Labs, Inc. did actually begin a Phase I clinical trial in patients with severe steroid-refractory Ulcerative Colitis as of July 9, 2002 as taught by "Protein Design Labs (PDLI) Begins Phase I Clinical Trial of Nuvion in Ulcerative Colitis," PRNewswire-FirstCall, July 9, 2002, pages 1-2. Thus, not do the applied references supply a reasonable expectation of success, but also one of ordinary skill in the art, prior to applicant's earliest claimed priority date, affirmed this reasonable expectation of success by investing time and expense to plan and carry out a phase I clinical trial.

Applicant further argues the instantly claimed method represents, "***an unexpected solution*** to the serious problem hitherto faced by patient with severe steroid refractory ulcerative colitis" in that "the present application provides data showing dramatic and durable effects from administration of the claimed antibodies to patients with severe steroid refractory ulcerative colitis."

Applicant's argument has been considered but has not been found convincing.

While it is not entirely clear what applicant means by "an unexpected solution to the serious problem hitherto faced...," insofar as applicant is arguing that the data presented in the instant specification shows an unexpected efficacy for the claimed method, applicant has not put forth objective evidence to establish that the result would actually be unexpected by the skilled artisan. For example, applicant has not put forth evidence comparing the alleged unexpected results to the closest prior art, and then explained why one of ordinary skill in the art would consider the data presented in the instant specification unexpected given their knowledge of the use of anti-CD3 + steroids to treat inflammatory conditions in the prior and the teachings of the applied references. IN the absence of such an argument, applicant has not rebutted the prima facie showing of unpatentability.

Along these lines, it is noted that according to MPEP § 2145, "arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.")."

Applicant further argues that claims 23 and 24 are further patentable due to the claimed low dosages.

To rebut a *prima facie* case of obviousness based on overlapping ranges, the MPEP at § 2144.05 teaches a showing of the criticality of the claimed range is required. "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)," and continues, "[a] *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. In re Geisler, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997)".

Applicant concedes that the claimed dosage ranges (e.g., "10 ug/kg or less; 15 ug/kg or less") overlap the teachings of Tso (e.g., "0.125 ug/kg – 1250 ug/kg; 1.25 ug/kg – 625 ug/kg; and 12.5 ug/kg – 125 ug/kg," based on an 80 kg patient), applicant argues that Tso's dosage ranges "are broad and not proposed specifically for treating ulcerative colitis, much less severe steroid refractory Ulcerative Colitis."

Applicant's argument has been considered but has not been found convincing, essentially for the reasons of record.

In particular, it noted that not only does Tso teach several dosage ranges that overlap the claimed ranges, but also as stated in the prior Office Action of January 9, 2007, Tso teaches that the effective dose of anti-CD3 is dependent upon "the severity of the condition and the general state of the patient's own immune system...", and that the dosage and scheduling of administration are ultimately "selected by the treating physician." (See, in particular, column 12, 3rd to 4th paragraphs). Therefore, the dosage of anti-CD3 antibody is a recognized results-effective variable, i.e., a variable that is recognized as important for therapeutic use of anti-CD3 antibody and is subject to optimization by routine experimentation by one of ordinary skill in the art, such a physician administering the claimed antibody to treat inflammatory bowel disease. See M.P.E.P. § 2144.05 II.B. and In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Applicant further attempts to show the claimed anti-CD3 antibody dosage ranges are not obvious over the prior art range by pointing to an applicant prepared compilation of dosages of various other antibody therapeutics.

However, applicant's evidence of "unexpected results" are not convincing for several reasons.

First, while applicant does not point this out, it appears that all of the antibodies listed in the table, other than the first entry, Orthoclone OKT3, target antigens other than CD3. Furthermore, most of the table entries do not indicate the intended patient population for the listed antibody nor is it readily ascertainable from the table or applicant's arguments if the antibodies shown are murine, chimeric, humanized, pegylated etc. Thus, applicant has provided a list of antibodies to diverse ligands involved in diverse diseases, and wherein the antibodies themselves may also have diverse properties due to structural differences. Thus, most of this information in this table does not appear to be relevant to any evidence of unexpected results of the claimed range, as it does not relate to the nearest prior art, absent an argument to the contrary.

Moreover, with respect to the single relevant antibody, Orthoclone OKT3, the Examiner submits that this is ***not*** the closest prior art that should be considered in light of, *inter alia*, that orthoclone OKT3 is a fully murine antibody (see OKT3 package insert cited by applicant) while the claimed antibody is humanized antibody with a genetically altered Fc for the specific purpose of preventing the cytokine release syndrome associated with OKT3. Thus, the two antibodies would be expected to have very different serum half lives and toxicities. Additionally, orthoclone may also bind to a different CD3 epitope than the claimed antibody.

Rather, in direct response to applicant's arguments and provision of evidence concerning unexpected results and Ulcerative Colitis clinical trials, the Examiner submits that Norman et al. (Transplantation. 2000 Dec 27;70(12):1707-12), is far closer prior art which teaches the results of a Phase I trial in which HuM291, an antibody which is substantially similar if not identical to the antibody of claims 15, 16, 17 and 19, was administered to human patients

with end-stage renal disease. (see entire document, in particular, Abstract and Introduction on pages 1707-1708). In this study it was found that patients receiving a single dose of 1.5 ug/kg achieved rapid, dose-dependent marked depletion of T cells, as did other cohorts of patients receiving 4.5 ug/kg and 15 ug/kg (see Materials and Methods, page 1708 and Results and Discussion, in particular page 1710, right column).

Given the effectiveness of dosages ranging from as low as 1.5 ug/kg to 15 ug/kg in patients with end-stage renal disease, one of ordinary skill in the art would not consider treating severe steroid refractory Ulcerative Colitis patients with 10 – 15 ug/kg or less anti-CD3 antibody to be an unexpected result.

In conclusion, when Applicant's arguments and objective evidence, and the data in the instant specification are taken as a whole and weighed against the evidence supporting the *prima facie* case of unpatentabililty, the instant claims, by a preponderance of evidence, remain unpatentable over Tso in view of Lobb, Rutgeerts, Banerjee and Strom. See M.P.E.P. § 716.01(d).

11. **New claims 27-30 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Tso et al. (U.S. Patent No. 5,834,597, cited in applicant's IDS of August 30, 2004) in view of Lobb et al. (U.S. Patent No. 5,932,214), Rutgeerts et al. (Eur J Surg. 1998 Dec;164(12):911-5), Banerjee et al. (USSN 10/622,932) Strom et al. (Therapeutic Immunology edited by Austen et al., Blackwell Science, Cambridge, MA, 1996; pages 451-456), and further in view of Norman et al. (Transplantation. 2000 Dec 27;70(12):1707-12, cited with applicant's IDS of April 5, 2007), as evidenced by Trajkovic V., (Current Opinion in Investigational Durgs 2002 3(3):411-414) and "Protein Design Labs (PDLI) Begins Phase I Clinical Trial of Nuvion in Ulcerative Colitis", (PRNewswire-FirstCall, July 9, 2002, pages 1-2).

as applied to claims 1, 4-8, 10-17, 19, 20 and 24-26 above in Section 6 above, ***and further in view of Carpenter et al.*** (Blood. 2002 Apr 15;99(8):2712-9, cited on applicant's IDS of April 5, 2007).

This is a New Grounds of Rejection, necessitated by applicant's addition of claims 27-30.

The teachings of Tso, Lobb, Rutgeerts, Banerjee, Strom, Norman, Trajkovic V., and "Protein Design Labs (PDLI) Begins Phase I Clinical Trial of Nuvion in Ulcerative Colitis,"

Moreover, it should be noted that in addition to the teachings of Tso given above and in previous Office Actions, Tso teaches that anti-CD3 can be administered via "***Single*** or multiple administrations on a daily, weekly or monthly schedule can be carried out with dose levels and pattern being selected by the treating physician." Thus, both the anti-CD3 dosage concentration AND the anti-CD3 dosage schedule are ***art recognized results-effective variable***, i.e., variables that are recognized as important for therapeutic use of anti-CD3 antibody and are subject to optimization by routine experimentation by one of ordinary skill in the art, such a physician administering the claimed antibody to treat inflammatory bowel

disease. See M.P.E.P. § 2144.05 II.B. and In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

That said, the claimed invention differ from the reference teachings given above in that the reference teachings do not explicitly recite that the course of treatment consists of a single administration of the antibody or of administration on two days.

However, given the teachings of Carpenter, one of ordinary skill in the art would have had a reasonable expectation of success in administering anti-CD3 antibody as a single dose therapy or over two days. In particular, Carpenter teaches that a single dose of the anti-CD3 antibody HuM291, which is substantially similar if not identical to the antibody of claims 15, 16, 17 and 19, was more effective in treating steroid-refractory acute graft-versus-host disease patients than was multiple smaller doses leading to a larger overall cumulative dose. (see, entire document, in particular Abstract, Introduction and Discussion, including page 2712 and 2718, left column). Carpenter concludes, "The structural features of visilizumab [HuM291] involved humanization...[t]he clinical data reported here support the concept that rational antibody engineering can provide rapidly acting, effective, and tolerable immunosuppression with ***convenient single-dose administration***." (see, in particular, page 2718, left column).

Moreover, one of ordinary skill in the art would have been motivated to administer anti-CD3 as a single dose rather than multiple smaller (which in addition actually require more cumulative dose for the same effect) not only for the obvious "convenience" to both physicians and patients noted by Carpenter, but also as has been long known and readily appreciated by one of ordinary skill in the art, to reduce the cost of manufacturing (less dose required per patient), administration (single doctor visit versus multiple visits) and packaging/mode of administration (it is easier, more precise, and more efficient to deliver one large volume than multiple small volumes).

Furthermore, it is noted that Tso recognizes anti-CD3 dosage concentration and schedule to be results-effective variables and provides guidance and direction for their optimization by routine experimentation as described above. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955), and see M.P.E.P. § 2144.05 II.A.

Thus, from the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention.

Accordingly, new claims 27-30 are rejected as unpatentable over Tso, Lobb, Rutgeerts, Banerjee, Strom, Norman, Trajkovic V., and "Protein Design Labs (PDLI) Begins Phase I Clinical Trial of Nuvion in Ulcerative Colitis," and further in view of Carpenter

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 4, 5, 10-17, 19, 20, 23 and 24-30 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13, 15, and 18-27 of copending Application No. 11/713, 465 in view of Lobb et al. (U.S. Patent No. 5,932,214), Rutgeerts et al. (Eur J Surg. 1998 Dec;164(12):911-5), Banerjee et al. (USSN 10/622,932) Strom et al. (Therapeutic Immunology edited by Austen et al., Blackwell Science, Cambridge, MA, 1996; pages 451-456), and further in view of Norman et al. (Transplantation. 2000 Dec 27;70(12):1707-12, cited with applicant's IDS of April 5, 2007), as evidenced by Trajkovic V., (Current Opinion in Investigational Drugs 2002 3(3):411-414) and "Protein Design Labs (PDLI) Begins Phase I Clinical Trial of Nuvion in Ulcerative Colitis", (PRNewswire-FirstCall, July 9, 2002, pages 1-2), and further in view of Carpenter et al. (Blood. 2002 Apr 15;99(8):2712-9).

This is a New Grounds of Rejection necessitated by a new application sharing an inventor with the present application being filed since the previous Office Action of January 9, 2007.

The instant claims differ from the reference claims in that the instant claims recite treatment of severe steroid resistant ulcerative colitis, recite measuring treatment as change in various scales, and recite various particular antibody sequences.

However, the reference claims either anticipate the instant claims because, while they may not be identical, they are not patentably distinct and/or render the instant claims obvious given the teachings of Lobb, Rutgeerts, Banerjee, Strom, Norman, Trajkovic V., "Protein Design Labs (PDLI) Begins Phase I Clinical Trial of Nuvion in Ulcerative Colitis," and Carpenter as described in Sections 6-7 above.

This is a provisional obviousness-type double patenting rejection.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on April 5, 2007 also prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a) and § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
July 6, 2007

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER